510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k060585

B. Purpose for Submission:
New Device

C. Measurand:
Adrenocorticotropic hormone (ATCH)

D. Type of Test:
Quantitative electrochemiluminescence immunoassay

E. Applicant:
ROCHE DIAGNOSTICS CORP.

F. Proprietary and Established Names:
Roche Elecsys-ACTH, ACTH CalSet, ACTH CalCheck, PreciControl ACTH

G. Regulatory Information:

1. Regulation section:
   21CFR §-862.1025-Adrenocorticotropic hormone (ACTH) test system.
   21 CFR §-862.1150-Calibrator.
   21 CFR §-862.1660-Quality control material (assayed and unassayed).
2. Classification:
   Class II
3. Product code:
   CKG - Radioimmunoassay, ACTH
   JIT- Calibrator, secondary
   JJX- Single (specified) analyte controls (assayed and unassayed)
4. Panel:
   Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See Indications for use
2. Indication(s) for use:
   Elecsys ACTH Assay:
   Immunoassay for the in vitro quantitative determination of adrenocorticotropic hormone (ACTH) in human EDTA plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E 170 (Elecsys module) immunoassay analyzers. ACTH measurements are used in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushings syndrome, adrenocortical insufficiency, and the ectopic ACTH syndrome.

   Elecsys ACTH CalSet is used for calibrating the quantitative Elecsys ACTH assay on the Elecsys immunoassay analyzers.

Elecsys ACTH CalCheck:
For use in the verification of the calibration established by the Elecsys ACTH reagent on Elecsys 1010/2010 and MODULAR E170 immunoassay analyzers.

Elecsys PreciControl ACTH is used for quality control of the Elecsys ACTH immunoassay on the Elecsys immunoassay analyzers.

3. Special conditions for use statement(s):
   For prescription use
4. Special instrument requirements:
   Roche Elecsys 1010/2010 and MODULAR ANALYTICS E 170

I. Device Description:

The Elecsys ACTH Assay consists of 3 wet reagents that include streptavidin-coated microparticles, biotinylated mouse monoclonal anti-ACTH antibody, ruthenium-labeled monoclonal mouse anti-ACTH antibody, buffer, and preservatives. Each kit includes reagents for 100 tests.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Immulite ACTH assay, Elecsys Prolactin II Cal Check, and Elecsys PreciControl Troponin T
2. Predicate 510(k) number(s):
   k960066, k053059, and k031990 respectively
3. Comparison with predicate:

Substantial equivalence – similarities

Immunoassay Comparison		
Feature	**Elecsys ACTH**	**Predicate Device Immulite ACTH Assay**
Intended Use	Immunoassay for the in vitro quantitative determination of adrenocorticotropic hormone (ACTH) in human EDTA plasma. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E 170 (Elecsys module) immunoassay analyzers.	For in vitro diagnostic use with the Immulite 2000 analyzer – for the quantitative measurement of adrenocorticotropic hormone in EDTA, plasma, as an aid in the assessment of adrenal insufficiency and hypersecretion.
Indication for Use	ACTH measurements are used in the differential diagnosis and treatment of certain disorders of the adrenal glands such as Cushings syndrome, adrenocortical insufficiency, and the ectopic ACTH syndrome.	As an aid in the assessment of adrenal insufficiency and hypersecretion.
Assay Protocol	Sandwich assay	Solid-phase, two site

Detection Protocol	Electrochemiluminescent Immunoassay	Chemiluminescent immunometric assay
Sample Type	Human plasma treated with K_3-EDTA	Human plasma treated with EDTA
Calibrator	ACTH CalSet	ACTH Adjustors (LACL, LACH)

CalSet Comparison		
Characteristic	**Elecsys ACTH CalSet**	**Predicate Device Immulite ACTH Assay**
Levels	Two	Same
Format	Lyophilized	Same

CalCheck Comparison		
Characteristic	**Elecsys ACTH CalCheck**	**Predicate Device Elecsys Prolactin II CalCheck**
Levels	Three	Same
Format	Lyophilized	Same
Stability	Unopened: Store at 2-8°C up to the printed expiration date on the bottle labels Reconstituted: 15 – 25 °C : 4 hrs	Same
PreciControl Comparison		
Characteristic	**Elecsys ACTH PreciControl**	**Predicate Device Elecsys PreciControl Troponin T**
Levels	Two	Same
Format	Lyophilized	Same
Handling	Dissolve carefully the contents of one bottle by adding exactly 2.0 mL of distilled water and allow to stand closed for 15 minutes to reconstitute. Mix carefully, avoiding the formation of foam.	Same

Substantial equivalence – differences

Immunoassay Comparison		
Feature	**Elecsys ACTH**	**Predicate Device Immulite ACTH Assay**
Calibration Interval	E170/Elecsys 2010: After 1 month (28 days) when using the same reagent lot. After 7 days (when using the same reagent kit on the analyzer). Elecsys 1010: With every reagent kit. After 7 days (20-25ºC). After 3 days (25-32ºC).	Every four weeks.
Platform	Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) analyzers.	Immulite 2000 Analyzer
Calibration Verification	ACTH CalCheck	None stated in the package insert.
Controls	PreciControl ACTH	LACCM: Bi-level ACTH control module (protein based).
Feature	**Elecsys ACTH**	**Predicate Device Immulite ACTH Assay**
Reagent Stability	Unopened: 2-8ºC - Up to the stated expiration date Opened: 2-8ºC - 12 weeks On the E170 / Elecsys 2010 – 4 weeks On the Elecsys 1010: – 4 weeks (stored alternately in the refrigerator and on the analyzer- ambient temperature 20-25ºC; up to 20 hours opened in total.)	ACTH Reagent Wedge: Stable at 2 – 8ºC until the expiration date.
Measuring Range	1 – 2,000 pg/mL	5 – 1,250 pg/mL

K. Standard/Guidance Document Referenced (if applicable):

CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline-Second Edition - EP05-A2

L. Test Principle:

Test principle

- Sandwich principle. Total duration of assay: 18 minutes.
- 1st incubation: 50 µL of sample, a biotinylated monoclonal ACTH-specific

antibody, and a monoclonal ACTH-specific antibody labeled with a ruthenium complexa react to form a sandwich complex.

- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.
- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:
   Reproducibility was determined using Elecsys reagents, pooled human plasma (HP) and controls (PC) in a modified protocol CLSI EP5-A: 6 times daily for 10 days (n = 60); within-run precision on MODULAR ANALYTICS E170 analyzer, n = 21. The following results were obtained:

Elecsys 1010/2010			**Within-run precision**			**Total precision**		
Sample	Mean pg/mL	pmol/L	SD pg/mL	pmol/L	CV %	SD pg/mL	pmol/L	CV %
HP 1	4.9	1.08	0.14	0.031	2.9	0.27	0.059	5.4
HP 2	74.2	16.3	1.45	0.319	2.0	1.75	0.385	2.4
HP 3	1390	306	29.8	6.56	2.1	36.2	7.97	2.6
PC ACTH1	115	115	1.76	0.388	1.5	1.96	2.18	1.7
PC ACTH2	970	214	15.9	3.50	1.6	17.6	3.88	1.8

MODULAR ANALYTICS E170										
	Within-run precision					**Total precision**				
Sample	Mean		SD		CV	Mean		SD		CV
	pg/mL	pmol/L	pg/mL	pmol/L	%	pg/mL	pmol/L	pg/mL	pmol/L	%
HP 1	4.9	1.08	0.13	0.03	2.7	4.96	1.09	0.266	0.059	5.4
HP 2	64.3	14.2	0.41	0.09	0.6	76.1	16.8	2.67	0.588	3.5
HP 3	1205	265	7.83	1.72	0.7	1444	318	53.6	11.8	3.7
PC ACTH1	111	24.4	0.70	0.15	0.6	114	25.1	2.09	0.460	1.8
PC ACTH2	968	213	11.4	2.51	1.2	972	214	19.1	4.2	2.0

b. *Linearity/assay reportable range:*
The reportable range of the assay is 1.0-2000 pg/mL (0.220-440 pmol/L). This range is defined by the lower detection limit and the maximum of the master curve. Values below the detection limit are reported as < 1.0 pg/mL (< 0.220 pmol/L). Values above the measuring range are reported as > 2000 pg/mL (> 440 pmol/L).
The sponsor demonstrated linearity of the assay up to 1766.7 pg/mL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Traceability: This method has been standardized gravimetrically with synthetic ACTH produced at Roche.

The CalSet, CalCheck and the PreciControl products are assayed and compared to reference preparations and target values and ranges are assigned. The values for ACTH are standardized against in-house reference standards (synthetic ACTH in analyte-free human plasma matrix).

Study 1: Accelerated Stability
The Elecsys ACTH calibrators were stored at 35°C for 3 weeks, the reference material at 4°C. At the end of three weeks, this on-test material was analyzed in duplicate along with a reference material. The recovery was calculated as a percent of the reference value.

Study 2: Reconstituted Stability at 20-25°C
The Elecsys ACTH calibrators were reconstituted and stored for 4 hours at 20-25°C. The respective reference material was stored at 4°C. At the end of storage time, the on-test material was analyzed in duplicate along with a reference material. The recovery was calculated as a percent of the reference value.

Study 3: Reconstituted Stability at -20°C:
The Elecsys ACTH calibrators were reconstituted and stored for 12 weeks at -20°C. The respective reference material was stored at 4°C. At the end of storage time, the on-test material was analyzed in duplicate along with a reference material. The recovery was calculated as a percent of the reference value.

The sponsor's acceptance criterion was recovery of signal 90 – 110% of the reference value.

ACTH CalCheck and PreciControl ACTH: followed the same study protocols as above. The sponsor's acceptance criterion was recovery of concentration 85 – 115% of the reference value.

d. *Detection limit:*
1.0 pg/mL (0.220 pmol/L)

The detection limit represents the lowest measurable analyte level that can be distinguished from zero (limit of the blank). It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1 + 2 SD, within-run precision, n = 21).

e. Analytical specificity:

The Elecsys ACTH two-site immunoassay measures intact ACTH 1-39. When ACTH fragments or peptides were added to a patient's plasma sample with defined ACTH concentration, no interference was observed with ACTH 1-10, ACTH 11-24, beta-MSH, and beta-Endorphin. Other ACTH fragments (ACTH 1-17, ACTH 1-24, ACTH CLIP 18-39, ACTH 22-39, alpha-MSH 1-13) > approx. 5000 pg/mL can bind to one of the antibodies and thereby negatively interfere with the sandwich formation and lead to lower ACTH values. See table below:

Cross-Reactant	**Concentration of cross-reactant [pg/mL]**	**Apparent ACTH [pg/mL]**	**Change in ACTH concentration [pg/mL]**	**% Cross-reactivity**
None (control)	0	44.1	--	--
ACTH 1-17	50000	10.6	-33.5	-0.07
	5000	36.9	-7.2	-0.14
	500	42.6	-1.5	-0.31
ACTH 1-24	50000	10.2	-33.8	-0.07
	5000	37.9	-6.2	-0.12
	500	42.5	-1.6	-0.32
ACTH 18-39	50000	2.0	-42.1	-0.08
	5000	14.9	-29.2	-0.58
	500	37.0	-7.0	1.41
ACTH 22-39	50000	0.00	-44.1	-0.09
	5000	6.3	-37.8	-0.76
	500	29.4	-14.7	-2.94
alpha MSH	50000	12.3	-31.8	-0.06
	5000	34.3	-9.8	-0.20
	500	41.3	-2.8	-0.56

Pro-opiomelanocortin (POMC - partially purified from an adenoma cell line) showed approximately 1.6% cross-reactivity at 1560 pmol/L.

The following pharmaceutical compounds were spiked into plasma samples and tested by the Elecsys ACTH on Elecsys 2010 Immunoassay Analyzer.

Each compound was found to be non-interfering at the concentration listed below.

Compound	Concentration
Acetaminophen	20 mg/L
Acetylcysteine	30 mg/L
Acetylsalicylic acid	300 mg/L
Ampicillin	200 mg/L
Ascorbic acid	30 mg/L
Ca- Dobesilate	20 mg/L
Cefoxitin	250 mg/L
Cyclosporine	1 mg/L
Doxycycline	10 mg/L
Heparin	10 U/mL
Ibuprofen	50 mg/L
Levodopa	4 mg/L
Methyldopa	2 mg/L
Metronidazole	10 mg/L
Phenylbutazone	100 mg/L
Rifampicin	20 mg/L
Theophylline	10 mg/L

The assay is unaffected by icterus (bilirubin < 25 mg/dL), hemolysis (Hb < 0.4 g/dL), lipemia (Intralipid < 1500 mg/dL), or biotin (< 60 ng/mL). Rheumatoid factor above 400 IU/mL may interfere with the assay results. The sponsor's acceptance criterion was recovery within ± 15% of initial value.

Studies evaluating high-dose hook effect demonstrated that samples containing ACTH concentrations up to $1*10^6$ pg/mL do not give falsely low results with this assay.

f. Assay cut-off:
Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:
A comparison of the Elecsys ACTH assay (y) with a commercially available ACTH test (x) using clinical samples gave the following regression statistics (units = pg/mL):
Number of samples measured: 180

Passing/Bablok	Linear regression
y=1.08x+1.23 τ = 0.898	y=0.90x+8.17 r = 0.992
SD (md68) = 2.55	Sy.x = 13.8

The sample concentrations were between 5.0 and 941 pg/mL (1.1 and 207 pmol/L).

b. Matrix comparison:

Not Applicable

3. Clinical studies:
   a. Clinical Sensitivity:
   Not Applicable

   b. Clinical specificity:
   Not Applicable

   c. Other clinical supportive data (when a. and b. are not applicable):
   Not Applicable

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range:
   Studies with the Elecsys ACTH assay using plasma samples from 354 apparently healthy adults gave the following results (5th-95th percentile):
   7.2-63.3 pg/mL (1.6-13.9 pmol/L)

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:
The submitted information in this premarket notification is complete and supports a substantial equivalence decision.